**Nervous System Development:**

Describe the Basic Germ Layers and tissues that contribute to the formation of structures found within the Peripheral portion of the nervous system and the Central portion of the nervous system.

AND

Describe the formation of the neural plate, neural groove, and neural tube. What induces or controls the development of these structures? How does the general development of the cranial portion of the tube differ from the development of the caudal potion of the tube?

AND

Describe the Development of the three developmental layers of the neural tube. What major areas of the nervous system are derived from each?

1. Gastrulation of the Embryo Occurs
   1. This creates the 3 germ layers
      1. Outer Layer = Ectoderm
      2. Middle Layer = Mesoderm
      3. Inner Layer = Endoderm
   2. Creates the Notochord
      1. Composed of Mesoderm cells
      2. Extends from mid anterior part of embryo to posterior part
      3. Formed as the embryo develops the primitive pit
         1. Primitive pit elongates to form the primitive streak
            1. Cells migrate thru this to form the mesoderm and notochord
      4. Defines the midline axis and helps create symmetry
      5. Important in the development of the rest of the nervous system
         1. Produces signals for early neural differentiation
            1. Signals to overlying neuroectoderm cells

Produces neural precursor cells

Called Neurulation

1. Neurulation
   1. Neuroectoderm
      1. Ectoderm immediately above the notochord
      2. Forms the entire nervous system
   2. Neuroectoderm thickens to become Neural Plate
      1. Columnar cells
   3. Margins of the plate fold inward
   4. Transforms the plate into the Neural Tube
      1. Will give rise to the brain and spinal cord
      2. Some cells of the neural tube = Neural Precursor Cells (Neural Stem Cells)
         1. Produce a lot of different types of cells
         2. Will eventually produce Neuroblasts
            1. Differentiate into Neurons
      3. Other cells
         1. Ventral midline cells
            1. Differentiated into epithelial-like Floorplate cells

Provides signals to help neuroblasts

Defines the dorsal-ventral polarity

Influences differentiation of neural precursor cells

Along with notochord signals causes differentiation of cells which will become spinal cord and hindbrain motor neurons

Sonic Hedgehog may be implicated in this process

* + - 1. Dorsal midline cells
         1. Differentiation into epithelial-like Roofplate cells

Signals cell differentiation

Differentiation into sensory relay neurons of the spinal cord and the hindbrain

* 1. Notochord, Roofplate, and Floorplate disappear when initial development is complete
  2. Neural Crest Cells
     1. At dorsal edges of the neural plate when both ends join
        1. Cells pinch off and form
     2. Migrate away from the neural tube
     3. Follow specific pathways to specific regions
     4. Give rise to a lot of cell types
        1. Peripheral potions of the nervous system (peripheral neurons and glia and autonomic structures)
        2. Also None-Nervous cells (such as melanocytes and adrenal medulla chromaffin cells)

Describe the formation of the alar plate and the basal plate. What major functional areas of the nervous system are derived from each?

1. Appearance of a longitudinal groove
   1. A grove on both sides of the Neural tube lumen appears as the neural tube grows
      1. The sulcus limitans
   2. Division of the Neural tube
      1. The sulcus limitans divides the neural tube into two portions
         1. Alar plate
            1. Gives rise to sensory neurons and interneurons of the spinal cord, medulla, pons, and mesencephalon
            2. Also gives rise to the diencephalon, cerebellum, and telencephalon
         2. Basal plate
            1. Gives rise to motor neurons and interneurons of the spinal cord, medulla, pons, and mesencephalon

Describe the positional changes that occur during the development of the spinal cord and vertebral column.

1. Spinal Cord Maintains the organization of the neural tube
   1. Spinal Cord Matures in rostral to caudal direction
   2. Cervical, thoracic, and upper lumbar segments develop from the neural tube by primary neurulation
   3. Lower lumbar, sacral, and coccygeal develop from secondary neurulation
   4. Ventricular Zone
      1. Adjacent to Central Canal
      2. Will produce the ependymal cells that line canal
   5. Intermediate/Mantle Zone
      1. Develops from the Basal and Alar plates
         1. Basal Plate Develops into the Ventral Grey
            1. Responsible for motor developments
         2. Alar Plate develops into the Dorsal Grey
            1. Responsible for sensory developments
   6. Lateral Zone/ Peripheral Marginal Zone
      1. Is outside the Mantle Zone
      2. Responsible for the development/location of ascending and descending tracts
   7. During the first trimester of pregnancy the spinal cord and vertebral column grow at the same rate
      1. After this trimester the vertebral column grows faster than the spinal cord
         1. Results in ending of the tip of the spinal cord at about L3 at birth
         2. The spinal roots once projected at right angles from the spinal cord through the vertebral foramen to form spinal nerves
            1. Now the roots have been dragged down by growth to form the cauda equine

Describe the Development of the lower portion of the brainstem.

AND

Describe the major features of the development of the Prosencephalon – Diencephalon and Telencephalon

AND

Summarize the functional components of the cranial nerves and localize (theoretically) their respective nuclei in the brainstem.

AND

Define and/or Describe the elements of the choroid plexus, tela choroidea, and arachnoid villi?.

AND

Differentiate between the tectum and the tegmentum of the brainstem.

AND

How does the structure of the Cerebellum reflect is phylogenetic development?

1. As the Neural Tube grows it begins to bulge out, constrict, and bend at certain regions
   * 1. The Luminal Spaces of the Neural Tube eventually become the ventricles
   1. Rostrally the neural tube forms a bulg
      1. Called the Prosencephalon
         1. Responsible for the development of the forebrain
   2. Just behind this is the sharpest bend
      1. The Cephalic Flexure
   3. Continuing Caudally there is another bulge
      1. The Mesencephalon
         1. Responsible for the development of the midbrain
   4. Caudal to that is another bulge
      1. The Rhombencephalon
         1. Responsible for the development of the hindbrain
   5. A final bend is at the end of the Rhombencephalon
      1. Called the Cervical Flexure
         1. Past this forms the precursor to the spinal cord
2. More growth and partitioning of the neural tube occurs
   * 1. Process is controlled by HOX Genes and the development of Neuromeres
   1. The Lateral aspects of the Prosencephalon form the telencephalon
      1. Forms two bilateral symmetric vesicles
         1. Have ventral and dorsal territories
            1. Dorsal Territory

Becomes the cerebral cortex and hippocampus

Has three zones

Ventricular zone

Some Cells migrate to the outer part of Mantle Zone from this zone

Forms the Cortical Plate

Becomes Lamina II to VI

Cells forming the layers migrate in an inward to outward fashion

Lamina I = Newest

Intermediate/Mantle Zone

Marginal Zone

Develops into Lamina I of cortex

* + - * 1. Ventral Territory (Basal Ganglia, Brainstem nuclei, and Olfactory bulb)

Ganglion Eminence

Becomes the Putamen and Caudate

Initially is one mass

Internal capsule develops and separates them

Also produces the Amygdala

External Globus Pallidus

Part from Ganglionic eminence

Part from Diencephalon

Incorporated into the telencephalon

Internal Globus Pallidus

Develops from the diencephalon

Incorporated into the telencephalon

* 1. Caudal portion of the Prosencephalon forms the diencephalon
     1. Becomes the Thalamus, Hypothalamus, Epithalmus, and the optic cups (retina and optic tract)
     2. Develops from the Alar Plate
     3. 3 swellings in the wall of the central canal
        1. Epithalamus
           1. Diminishes in size
        2. Thalamus
           1. Grows
        3. Hypothalamus
           1. Grows
     4. Central Canal becomes the 3rd Ventricle
  2. Dorsal portion of the Mesencephalon becomes the superior and inferior colliculi
     1. Is known as the tectum
        1. Is a derivative of the Alar Plate
  3. Ventral portion of the Mesencephalon becomes the midbrain tegmental nuclei
     1. Is known as the Tegmentum and composed of a number of structures
        1. Oculomotor Nucleus
        2. Trochelar Nucleus
        3. Substantia Nigra
        4. Red Nucleus
     2. Derived from the Basal Plate
     3. Mesencephalic Thickening creates the Cerebral Aqueduct
  4. Rostral portion of the Rhombencephalon becomes the Metencephalon
     1. Becomes the Cerebellum and Pons
  5. The Caudal portion of the Rhombencephalon becomes the myelencephalon
     1. Becomes the Medulla
     2. At the Juncture with the spinal cord the central canal opens to become the fourth ventricle
        1. Pushes the alar plate dorsolaterally
           1. Results in lateral or dorsolateral location of sensory neurons with respect to the basal plate motor neurons
     3. Thin layer of pia and ependymal cell roof plate is also formed
        1. Supported by richly vascularized Mesenchymal tissue the Tela Choroidea
        2. This ependymal cell layer eventually becomes the Choroid plexus
        3. Same type of development happens in the Diencephalon and Telencephalon to create the 3rd and Lateral Ventricles
     4. The sulcus limitans is retained and separates the alar and basal areas
        1. Found in floor of the 4th ventricle
     5. This same pattern of development is MAINTAINED IN THE PONS

1. Cerebellum Development
   1. Develops from the Metencephalon
   2. Develops from the dorsolateral portion of the alar plate of the 4th ventricle
      1. Grows outward to form the hemispheres and then inward to form the vermis
         1. Develops in the roof of the fourth ventricle
2. Cranial Nerve Nuclei
   1. Alar Plate
      1. Spinal Trigeminal Nucleus
      2. Sensory Trigeminal Nucleus
      3. Nucleus Solitarius
      4. Vestibular Nucleus
      5. Cochlear Nucleus
   2. Other Alar Plate Structures
      1. Inferior Olivary Nucleus
      2. Pontine Nuclei
   3. Basal Plate
      1. Hypoglossal Nucleus
      2. Nucleus Ambiguous
      3. Dorsal Motor Nucleus of Vagus
      4. Inferior Salvitory Nucleus
      5. Abducens
      6. Superior Salvitory Nucleus
      7. Trigeminal Motor
      8. Facial Motor Nucleus
3. Commissural Development
   1. Corpus Callosum, Anterior Commissure, and Fornix
      1. Arise from the Lamina Terminalis
         1. Small thickening appears in the lamina
            1. Right in front of interventricular foramen
            2. Lower portion separates

Forms the Anterior Commissure

* + - * 1. Upper part grows with the cerebral hemispheres

Forms two types of fibers

Transverse Fibers

Form dorsally and makes the Corpus Callosum

Longitudinal Fibers

Forms ventrally and makes the fornix

Passes to hippocampus and mammillary bodies

* + - * 1. A small anterior portion is left uninvaded by fibers and is stretched to become the septum pellucidum

What is the origin of the Cells of the Sympathetic Nervous System? How does this contrast with the origin of the parasympathetic system?????

1. I don’t know

Describe the Morphological defects and developmental errors associated with:

1. Spina Bifida
   1. Caused by incomplete closure of the embryonic Neural Tube
   2. Some vertebrae covering the spinal cord remain unfused or open
      1. Meningocoele
         1. Least common form
         2. The meninges are forced between the gaps between the vertebrae
      2. Myelomeningocoele
         1. Common
         2. Serious
         3. Spinal cord protrudes through an opening in the vertebral column
         4. Meninges form a sac over the spinal cord
         5. Susceptible to life threatening infections
2. Myeloschisis
   1. Failure of the neural plate to fuse and form a complete neural tube
   2. Spina bifida is inevitable in this case
3. Meroanencephaly (anencephaly)
   1. Meroanencephaly
      1. Brain and cranium present in basic form
   2. Anencephaly
      1. Cephalic end of the neural tube fails to close
      2. Results in the absence of major portions of brain, skull, and scalp
4. Hydrocephalus
   1. Abnormal Accumulation of CSF
   2. Caused by a blockage of outflow for CSF
   3. Can be treated by placing a ventricular shunt
5. Menigoencephalocele
   1. Protrusion of the meninges and the brain due to a congenital cranial defect
6. Arnold-Chiari Malformation
   1. Downward displacement of the cerebellar tonsils through the foramen magnum
   2. Can cause hydrocephalus
7. Hydranencephaly
   1. Cerebral Hemispheres are absent
   2. Replaced by sacs filled with cerebral spinal fluid
8. Mental retardation
   1. Generalized disorder characterized by significant impairment of cognitive function
   2. Many different cause
      1. Genetics, drugs, deficiencies during development, etc

Describe the relationships and importance of Neural Crest Cells in relation to:

1. Origin
   1. At lateral edges of neural plate
      1. When plate joins these cells form & pinch off dorsally from neural tube
   2. Migrate away from the neural tube
2. Relation to HOX 2 Genes
   1. HOX genes (Homeobox genes) are expressed segmentally
   2. HOX gene expression does not extend into the midbrain or forebrain
   3. These contribute to the segmentation of the body and may contribute to signaling of neural crest cells
3. Distribution – migration (head vs. body)
   1. Craniofacial Neural crest cells
      1. Contribute to craniofacial mesenchyme
      2. Develops into various cranial ganglia, cartilage, bone, thymus, bones of middle ear, bones of jaw, teeth
   2. Trunk Neural crest cells
      1. Develops into melanocytes
      2. Develops into dorsal root ganglion, sympathetic ganglion, Adrenal medulla (chromaffin cells), and nerves surrounding the aorta
   3. Vagal and Sacral Neural crest cells
      1. Develop into ganglia of the enteric nervous system and parasympathetic ganglia
   4. Cardiac Neural crest cells
      1. Develops into melanocytes, cartilage, connective tissue, musculo-connective tissue of large arteries, septum dividing pulmonary trunk from aorta, and semilunar valves
4. Diseases Associated with neural crest cells:
   1. Hirschsprung’s Disease
      1. Results from the loss of neural crest cells that make up the myenteric plexus of the gut
      2. Results in colon hypertrophy/distention and feces retention
   2. Waardenburg syndrome
      1. Caused by neural crest defects and pigmentation anomalies
      2. Causes minor defects
         1. Example: medial white forelock
   3. DiGeorge Syndrome
      1. Genetically inherited
         1. Caused by deletions
      2. Migration defects of neural crest cells
      3. Affects the thymus
   4. Neurofibromatosis
      1. Genetically Inherited
         1. Autosomal dominant
      2. Neural tissue grows tumors
      3. Affects all neural crest cell derivative (Schwann cells, melanocytes, and endoneurial fibroblast)
      4. Also results in altered skin pigmentation (café Alulae spots)
   5. Albanism
      1. Complete loss of pigmentation
      2. Results in loss of enzymes to produce pigment in melanocytes
         1. Derivatives from neural crest cells
   6. Pheochromocytosis
      1. Tumor of the adrenal medulla
         1. Originating in the chromaffin cells
            1. Neural crest derivatives
   7. Neuroblastoma
      1. Most common extracranial solid cancer in children
      2. Is a neuroendocrine tumor
      3. Arises from neural crest derivatives of the sympathetic nervous system